

SEQUENCE LISTING

<110> WALLACH, David
 GOLTSEV, Yura
 KOVALENKO, Andrei
 VARFOLOMEEV, Eugene
 BRODIANSKI, Vadim

<120> CASH (CASPASE HOMOLOGUE) WITH DEATH EFFECTOR DOMAIN,
 MODULATORS OF THE FUNCTION OF FAS RECEPTORS

<130> WALLACH=23

<140> 09/380,546

<141> 1999-11-29

<150> PCT/IL98/00098

<151> 1998-02-26

<150> IL 120367

<151> 1997-03-03

<150> IL120759

<151> 1997-05-01

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<170> PatentIn Ver. 2.0

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Gly Ala Gly Thr Ser Tyr Arg Asn Val Leu Gln Ala Ala Ile Gln Lys
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His Cys Pro Asp Leu Lys Ile Leu Gly Asn Cys Ser Met
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Phe Asp Leu Leu Lys Arg Ile Leu Lys Met Asp Arg Lys Ala Val Glu
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Ile Phe Leu Met Lys Asp Tyr Met Gly Arg Gly Lys Ile Ser Lys Glu
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Lys Ala Thr Val Glu Asp His Leu Arg Arg Asn Pro His Leu Val Ser
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 Gln Lys Tyr Thr Gln Ser Ser Gln Gly Ala Arg Ser Asn Met Asn Thr
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 Pro Pro His Ile Arg Glu Glu Thr Tyr Arg Met Gln Ser Lys Pro Leu
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 Gly Ile Cys Leu Ile Ile Asp Cys Ile Gly Asn Asp Thr Lys Tyr Leu
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 Ala Gln His Gln Asp Tyr Asp Ser Phe Ala Cys Val Leu Val Ser Leu
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Ser Lys Cys Lys Leu Asp Asp Asp Met Asn Leu Leu Asp Ile Phe Ile
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Asp Tyr Glu Glu Phe Ser Lys Glu Arg Ser Ser Ser Leu Glu Gly Ser
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Pro Asp Glu Phe Ser Asn Gly Glu Glu Leu Cys Gly Val Met Thr Ile
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Val Tyr Gln Met Lys Ser Lys Pro Arg Gly Tyr Cys Leu Ile Ile Asn
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 Cys Thr Lys Glu Glu Val Glu Arg Leu Leu Pro Thr Arg Gln Arg Val
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 Gly Leu Cys Val Ile Val Asn Asn His Ser Phe Thr Ser Leu Lys Asp
 245 250 255
 Arg Gln Gly Thr His Lys Asp Ala Glu Ile Leu Ser His Val Phe Gln
 260 265 270
 Trp Leu Gly Phe Thr Val His Ile His Asn Asn Val Thr Lys Val Glu
 275 280 285
 Met Glu Met Val Leu Gln Lys Gln Lys Cys Asn Pro Ala His Ala Asp
 290 295 300
 Gly Asp Cys Phe Val Phe Cys Ile Leu Thr His Gly Arg Phe Gly Ala
 305 310 315 320

Val	Tyr	Ser	Ser	Asp 325	Glu	Ala	Leu	Ile	Pro 330	Ile	Arg	Glu	Ile	Met 335	Ser
His	Phe	Thr	Ala 340	Leu	Gln	Cys	Pro	Arg 345	Leu	Ala	Glu	Lys	Pro 350	Lys	Leu
Phe	Phe	Ile 355	Gln	Ala	Cys	Gln	Gly 360	Glu	Glu	Ile	Gln	Pro 365	Ser	Val	Ser
Ile	Glu 370	Ala	Asp	Ala	Leu	Asn 375	Pro	Glu	Gln	Ala	Pro 380	Thr	Ser	Leu	Gln
Asp 385	Ser	Ile	Pro	Ala	Glu 390	Ala	Asp	Phe	Leu	Leu 395	Gly	Leu	Ala	Thr	Val 400
Pro	Gly	Tyr	Val	Ser 405	Phe	Arg	His	Val	Glu 410	Glu	Gly	Ser	Trp	Tyr 415	Ile
Gln	Ser	Leu	Cys 420	Asn	His	Leu	Lys	Lys 425	Leu	Val	Pro	Arg	His 430	Glu	Asp
Ile	Leu	Ser 435	Ile	Leu	Thr	Ala	Val 440	Asn	Asp	Asp	Val	Ser 445	Arg	Arg	Val
Asp	Lys 450	Gln	Gly	Thr	Lys	Lys 455	Gln	Met	Pro	Gln	Pro 460	Ala	Phe	Thr	Leu
Arg 465	Lys	Lys	Leu	Val	Phe 470	Pro	Val	Pro	Leu	Asp 475	Ala	Leu	Ser	Ile	

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<211> 249
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<213> Homo sapiens
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Gly	Leu	Cys	Ile	Ile	Ile	Asn	Asn	Lys	Asn	Phe	His	Lys	Ser	Thr	Gly	
			20					25					30			
Met	Thr	Ser	Arg	Ser	Gly	Thr	Asp	Val	Asp	Ala	Ala	Asn	Leu	Arg	Glu	
		35					40					45				
Thr	Phe	Arg	Asn	Leu	Lys	Tyr	Glu	Val	Arg	Asn	Lys	Asn	Asp	Leu	Thr	
	50					55					60					
Arg	Glu	Glu	Ile	Val	Glu	Leu	Met	Arg	Asp	Val	Ser	Lys	Glu	Asp	His	
65					70					75					80	
Ser	Lys	Arg	Ser	Ser	Phe	Val	Cys	Val	Leu	Leu	Ser	His	Gly	Glu	Glu	
				85					90					95		
Gly	Ile	Ile	Phe	Gly	Thr	Asn	Gly	Pro	Val	Asp	Leu	Lys	Lys	Ile	Thr	
			100					105					110			

Asn Phe Phe Arg Gly Asp Arg Cys Arg Ser Leu Thr Gly Lys Pro Lys
 115 120 125
 Leu Phe Ile Ile Gln Ala Cys Arg Gly Thr Glu Leu Asp Cys Gly Ile
 130 135 140
 Glu Thr Asp Ser Gly Val Asp Asp Asp Met Ala Cys His Lys Ile Pro
 145 150 155 160
 Val Asp Ala Asp Phe Leu Tyr Ala Tyr Ser Thr Ala Pro Gly Tyr Tyr
 165 170 175
 Ser Trp Arg Asn Ser Lys Asp Gly Ser Trp Phe Ile Gln Ser Leu Cys
 180 185 190
 Ala Met Leu Lys Gln Tyr Ala Asp Lys Leu Glu Phe Met His Ile Leu
 195 200 205
 Thr Arg Val Asn Arg Lys Val Ala Thr Glu Phe Glu Ser Phe Ser Phe
 210 215 220
 Asp Ala Thr Phe His Ala Lys Lys Gln Ile Pro Cys Ile Val Ser Met
 225 230 235 240
 Leu Thr Lys Glu Leu Tyr Phe Tyr His
 245

<210> 9
 <211> 300
 <212> PRT
 <213> Homo sapiens

<400> 9
 Gln Gly Val Leu Ser Ser Phe Pro Ala Pro Gln Ala Val Gln Asp Asn
 1 5 10 15
 Pro Ala Met Pro Thr Ser Ser Gly Ser Glu Gly Asn Val Lys Leu Cys
 20 25 30
 Ser Leu Glu Glu Ala Gln Arg Ile Trp Lys Gln Lys Ser Ala Glu Ile
 35 40 45
 Tyr Pro Ile Met Asp Lys Ser Ser Arg Thr Arg Leu Ala Leu Ile Ile
 50 55 60
 Cys Asn Glu Glu Phe Asp Ser Ile Pro Arg Arg Thr Gly Ala Glu Val
 65 70 75 80
 Asp Ile Thr Gly Met Thr Met Leu Leu Gln Asn Leu Gly Tyr Ser Val
 85 90 95
 Asp Val Lys Lys Asn Leu Thr Ala Ser Asp Met Thr Thr Glu Leu Glu
 100 105 110
 Ala Phe Ala His Arg Pro Glu His Lys Thr Ser Asp Ser Thr Phe Leu
 115 120 125

Val	Phe	Met	Ser	His	Gly	Ile	Arg	Glu	Gly	Ile	Cys	Gly	Lys	Lys	His
130						135					140				
Ser	Glu	Gln	Val	Pro	Asp	Ile	Leu	Gln	Leu	Asn	Ala	Ile	Phe	Asn	Met
145					150					155					160
Leu	Asn	Thr	Lys	Asn	Cys	Pro	Ser	Leu	Lys	Asp	Lys	Pro	Lys	Val	Ile
				165					170					175	
Ile	Ile	Gln	Ala	Cys	Arg	Gly	Asp	Ser	Pro	Gly	Val	Val	Trp	Phe	Lys
			180					185						190	
Asp	Ser	Val	Gly	Val	Ser	Gly	Asn	Leu	Ser	Leu	Pro	Thr	Thr	Glu	Glu
		195					200					205			
Phe	Glu	Asp	Asp	Ala	Ile	Lys	Lys	Ala	His	Ile	Glu	Lys	Asp	Phe	Ile
	210					215					220				
Ala	Phe	Cys	Ser	Ser	Thr	Pro	Asp	Asn	Val	Ser	Trp	Arg	His	Pro	Thr
225					230					235					240
Met	Gly	Ser	Val	Phe	Ile	Gly	Arg	Leu	Ile	Glu	His	Met	Gln	Glu	Tyr
				245					250					255	
Ala	Cys	Ser	Cys	Asp	Val	Glu	Glu	Ile	Phe	Arg	Lys	Val	Arg	Phe	Ser
			260					265					270		
Phe	Glu	Gln	Pro	Asp	Gly	Arg	Ala	Gln	Met	Pro	Thr	Thr	Glu	Arg	Val
		275					280					285			
Thr	Leu	Thr	Arg	Cys	Phe	Tyr	Leu	Phe	Pro	Gly	His				
	290					295					300				

<210> 10

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:fluorogenic substrate

<220>

<223> Asp at position 1 is modified with an acetyl group; Asp at position 4 is modified with an a-(4-methyl-coumaryl-7-amide) group

<400> 10

Asp Glu Val Asp

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<210> 11

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PCR primer

<220>

<223> Tyr at position 1 is modified with an acetyl group; Asp at position 4 may be modified with a CH₂OC(O)-[2,6(CF₃)₂] Ph group or an a-(4-methyl-coumaryl-7-amide) group.

<400> 11

Tyr Val Ala Asp

1

<210> 12

<211> 37

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PCR primer

<400> 12

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37

<210> 13

<211> 22

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PCR primer

<400> 13

aagtgagcag atcagaattg ag

22

<210> 14

<211> 20

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PCR primer

<400> 14

gactcgagtc tagagtcgac

20

<210> 15

<211> 31

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PCR primer

<400> 15
gaggatcccc aaatgcaaac tggatgatga c 31

<210> 16
<211> 24
<212> DNA
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<220>
<223> Description of Artificial Sequence: PCR primer

<400> 16
gccaccagct aaaaacattc tcaa 24

<210> 17
<211> 31
<212> DNA
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<220>
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<400> 17
ttggatccag atggacttca gcagaaatct t 31

<210> 18
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<212> DNA
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<220>
<223> Description of Artificial Sequence: PCR primer

<400> 18
attctcaaac cctgcatcca agtg 24

<210> 19
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer

<400> 19
ggcttctcgt gggtcccaga gc 22

<210> 20
<211> 21
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: PCR primer

<400> 20

tgctcttcct gtgtagagat g

21